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ORIGINAL ARTICLE

The fetal profile line: a proposal for a sonographic reference line to classify forehead and mandible anomalies in the second and third trimester

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ABSTRACT

Objectives To test the fetal profile (FP) line, defined as the line that passes through the anterior border of the mandible and the nasion, as a reference line for forehead and mandible anomalies.

Methods Volumes of 248 normal and 24 pathological fetuses (16–36 and 19–37 weeks' gestation, respectively) were analysed retrospectively. When the FP line passes anteriorly, across or posteriorly to the frontal bone, this was defined as 'negative', 'zero' or 'positive', respectively. When the FP line was positive the distance (*F* distance) between the FP line and the frontal bone was measured.

Results No cases with a negative FP line were found in the normal fetuses. Before 27 weeks' gestation the FP line was always 'zero' except in one case. After 27 weeks' gestation the FP line was 'positive' in up to 25% (*F* distance (mean, range): 2.8, 2.1–3.6 mm). The FP line correctly identified 13 cases with retrognathia, 5 cases with frontal bossing and 3 cases with a sloping forehead.

Conclusion Although large prospective studies are needed, the FP line may be a useful tool to detect second trimester profile anomalies such as retrognathia, sloping forehead and frontal bossing with the possibility of quantifying the latter. © 2012 John Wiley & Sons, Ltd.

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Supporting information may be found in the online version of this article.

INTRODUCTION

Of all ultrasound images, the fetal face and especially the profile is highly appreciated by parents and frequently sought after by sonographers. Many abnormalities of the profile such as retrognathia, bossing or sloping forehead are associated with a wide range of genetic conditions and syndromes.^{1–5}

When multiple anomalies or markers are present, the recognition of specific features typical of a syndrome can be of crucial importance for optimal parental counselling and for further management of the pregnancy.

Although it is to be expected that the experienced sonographer will notice facial dysmorphisms, less experienced sonographers may benefit from objective measurements. Furthermore, the use of objective measurements creates the opportunity to document, communicate, compare, classify and follow-up findings.

The fetal profile is a tremendous source of information and therefore attempts should be made to find a simple approach

capable of translating the information it contains into simple lines and measurements. This may seem a challenge, owing to the complex curved nature of the fetal profile.

The aim of the present study was to develop and evaluate an easily applicable line, which we named the fetal profile (FP) line, as a potential new reference to identify and quantify forehead and mandible anomalies (Figure 1). The FP line was applied to three-dimensional volumes of normal second and third trimester fetuses (cross-sectionally and longitudinally). We also tested the proposed FP line retrospectively in pathological cases.

MATERIAL AND METHODS

The study was approved by the local ethics committee and all participants gave written consent. Study data were obtained from 272 (261 for cross-sectional and 11 for longitudinal study), nonsmoking, healthy, low-risk, pregnant Caucasian women with a singleton and uncomplicated pregnancy. Women were



Figure 1 Multiplanar view of a normal fetus showing the fetal profile (FP) line in box B and identification of the landmark used for the mandible (i.e. the middle point of the anterior border) with marker dot in the C-box

recruited at the time of the dating or routine second-trimester anomaly scan. They were asked to attend an additional examination between 16 and 36 weeks' gestation. Eleven healthy Caucasian employees of our hospital attended every 4 weeks, starting at 16 weeks' gestation, for a longitudinal study. Fetuses were excluded when a structural anomaly was found on ultrasound. Gestational age was determined from the last menstrual period and by a first trimester dating scan. The examinations were carried out transabdominally, using a General Electric Voluson 730 Expert ultrasound system (GE Medical Systems, Kretz Ultrasound, Zipf, Austria) equipped with a 2 to 5 MHz or 4 to 8 MHz abdominal transducer.

When the fetus was facing the transducer with closed mouth, at least two volumes of the fetal head were acquired, starting at the midsagittal plane. The ultrasound image of the fetal head was enlarged to at least one third the size of the screen, the render box was positioned to include the whole fetal head and the angles of the volume were adjusted to the size of the fetal head. Volumes were obtained with high-2 or maximum

quality depending on the behavioural state of the fetus. A normal frequency range was used in most women, but this was changed to 'resolution' or 'penetration' in case of a slim or obese woman. Except in the longitudinal group, each fetus was investigated only once for the purpose of this study.

All examinations were carried out by one experienced sonographer (EJP). The volumes were stored on removable digital media for subsequent analysis on 4D View software version 10.2 (GE Medical Systems, Kretz Ultrasound, Zipf, Austria). With the multiplanar mode the exact midsagittal plane was depicted as follows: initially the multiplanar images were rotated to obtain symmetrical views of the orbits. The reference dot was then placed at equal distance from the inner border of the orbits in the axial and coronal images, resulting in the exact midsagittal image in the original profile view.

The FP line was defined as the line that passes through the middle point of the anterior border of the mandible and the nasion (Figure 1). The nasion is the most anterior point at the intersection of the frontal and nasal bones. When necessary the marker dot in the C-box was used to identify the landmark on the mandible (Figure 1). Volume contrast imaging was used where necessary to improve the image quality.

When the FP line passed the frontal bone anteriorly its position was called 'negative' (Figures 2(as) and (ar)). When the FP line passed lengthwise through the frontal bone, this was called 'zero' (Figure 2(b)) and the length of the FP line passing through the frontal bone was measured. When the FP line passed the frontal bone posteriorly, its position was called 'positive' and the largest distance (F distance) from the FP line to the outer border of the frontal bone could be measured (Figure 2(c)). The F distance was measured perpendicular on the FP line.

Intraobserver and interobserver variability of the F distance was assessed by the intraclass correlation coefficient (ICC) on paired volumes acquired by the 4 to 8 MHz transducer from 15 patients with at least 3 days between the two assessments.

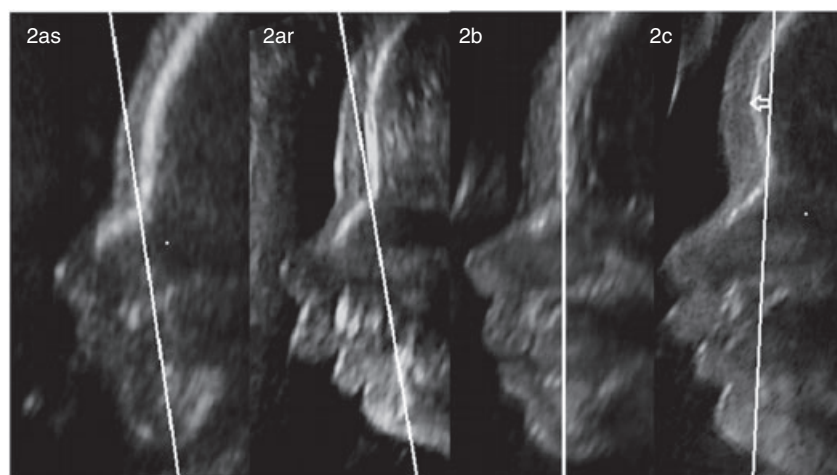


Figure 2 Ultrasound pictures showing examples of the 3 types FP lines. (as) and (ar), FP line is negative; (b) FP line is zero; (c) FP line is positive. Arrow indicates F distance. Fetus in picture (as) had a sloping forehead (case with trisomy 13), fetus in picture (ar) has retrognathia (case with Pierre Robin sequence), the other two fetuses are normal (case (b) at 25 weeks gestational age and case (c) at 32 weeks gestational age)

Subsequently, the FP line was tested retrospectively on stored three-dimensional volumes of fetuses that were suspected to have a facial anomaly or syndrome with specific facial features. All children born in this group were evaluated by an experienced neonatologist and when necessary by geneticists and dysmorphologists at a university centre.

Data were analysed using the statistical software SPSS version 17.0 for Windows (SPSS Inc., Chicago, IL, USA) and Microsoft Excel for Windows 2010. Means with ranges or percentage were calculated. Fisher's exact test was used to compare groups. $P \leq 0.05$ was considered statistically significant.

RESULTS

The cross-sectional study group included 261 fetuses. Two fetuses were excluded because an anomaly was diagnosed (spina bifida and facial cleft). In 16 fetuses no volume could be obtained because the fetus had an unfavourable position. Six cases were excluded from analysis because of uncertainty over mouth closure (one case), because extreme flexion of the head prevented identification of the mandibular landmark (one case) and because the forehead was not clearly visible (four cases). The FP line was tested in 237 fetuses cross-sectionally and in 11 fetuses longitudinally. Forty-nine investigations (20%) were performed with the 2 to 5 MHz transducer and 199 investigations (80%) with the 4 to 8 MHz transducer.

The mean body mass index of the women before pregnancy was 23.7 (range, 17.4–36.2). The mean amniotic fluid index was 17.1 (range, 7.3–28.3). The position of the fetus was cephalic in 67%, breech in 28% and transverse in 5%. The mean birth weight of the babies was 3472 g (range, 1160–4885 g) with 89% of the babies between the 5th and 95th percentile. Of the babies, 53% were boys and 47% girls.

The ICC for the F distance was 0.96 for both intraobserver and interobserver variability.

Cross-sectional group

There were no cases with a negative FP line. The FP line was zero in 222 cases (93.7%). The mean length of the FP line passing through the frontal bone was 15.6 mm (range, 5.1–31.6 mm). The FP line was positive in only 15 cases (6.3%); this never occurred before 27 weeks' gestation. The mean F distance was 2.8 mm (range, 2.1–3.6 mm). Most commonly seen was an FP line with position zero (>75% for each gestational week). The position of the FP line was not different between male and female fetuses, nor between fetuses in cephalic and breech or transverse position ($P = 0.26$ and 1.0, respectively).

Longitudinal group

In all 11 cases, at least four measurements were performed. All the measurements were within the normal range (established in the cross-sectional group) except in one case, where the FP line had already changed to positive already at 20 4/7 weeks' gestation. A normal boy was born in this case. In 7 of the 11 longitudinal cases the FP line remained zero throughout pregnancy. In four cases the FP line changed during

pregnancy, these changes were always from zero to positive and never the other way around.

Pathological group

The pathological group consisted of 24 cases. They are summarised in Table 1.

In 16 cases the ultrasound investigation raised the suspicion of retrognathia. In 13 of the 16 cases a negative FP line was found and in each of these cases retrognathia was confirmed after birth (Figure 2(ar)). Three of the 16 cases had a normal FP line position and retrognathia was not confirmed after birth.

In six cases ultrasound examination yielded a suspicion for bossing forehead (case 17–22). In five cases (case 17–21) the FP line was positive with an increased F distance (positive before 27 weeks or more than 3.6 mm after 27 weeks). A bossing forehead was confirmed in these five cases. In case 22 the measurements of the femur and humerus were < P3, there was a large amount of amniotic fluid (amniotic fluid index 270 mm) and the forehead seemed a little bossing (Figure 2(c)). The FP line position was normal and a healthy but dysmature child was born.

In two cases with suspicion of microcephaly (case 16, 23) the FP line was negative. Microcephaly was confirmed in both cases. Case 24 was diagnosed with microphthalmia, cerebellar and corpus callosum hypoplasia. The FP line was clearly negative (Figure 2(as)). Head circumference measurement was at the 5th percentile. Trisomy 13 was diagnosed and the pregnancy was a terminated.

DISCUSSION

We have described the fetal profile line as a possible tool for identifying profile anomalies. The FP line traces the frontal border of the mandible, the nasion and has, especially before 27 weeks, a stable relationship with the forehead. The FP line is the first objective tool for possible assessment of a sloping forehead.

We showed that before 27 weeks the forehead of almost all fetuses is straight and the FP line is aligned with the lower part of the frontal bone for at least 5 mm. We suggest that no further measurements are needed when the FP line has position zero. This line should therefore be easy to apply as a screening tool during a second trimester fetal anatomic survey. After 27 weeks the forehead changes to a curved shape with a positive FP line position in up to 25% of the cases. The shape of the forehead is not affected by the sex or the position of the fetus and we assume that the shape is determined by normal genetic anatomic predisposition.

Closure of the gap between the frontal bones with delineating of the metopic suture starts at around 16 weeks. At 32 weeks there is apparently closure of the metopic suture.⁶ In our series in almost all cases an ossification line was visible, indicating that the ultrasound beam is wider than the metopic suture or sufficient ossification has taken place to depict the bony forehead. In a few cases a thin echogenic line indicated the position of the future bony forehead and could easily be used as a landmark.

The landmark on the mandible was sometimes difficult to delineate because of shadowing. With multiplanar mode and the marker dot it was possible to identify this landmark in most cases (Figure 1).

Table 1 Summary of pathological cases

Nr	GA (weeks)	PF line ^a	Retro-grathia ^b	Bossing forehead ^b	Micro-cephaly ^b	Postnatal diagnosis	Other findings (detected by ultrasound, postpartum evaluation or pathology)	Genetic confirmation
1	37 1/7	0	—	—	—	normal	polyhydramnios	No
2	20	0	—	—	—	trisomy 18	small nose, cleft palate, CDH, AVSD, crossed fingers, rocker-bottom feet	Yes
3	28 6/7	0	—	—	—	CHARGE association	hemifacial microsomia, unilateral microphthalmia, horseshoe kidney	Yes
4	21 6/7	neg	R	—	—	14q11.2 deletion	hypoplastic aortic arch, LVOTO, perimembranous VSD,	Yes
5	21 4/7	neg	R	—	—	Goldenhar syndrome	hemifacial microsomia, unilateral microphthalmia, unilateral cleft lip, bilateral cleft palate, abnormal ear, heart defect (not specified), hemivertebrae	No
6	25 4/7	neg	R	—	—	Pierre Robin syndrome	cleft palate, malalignment VSD	No
7	26 6/7	neg	R	—	—	Pierre Robin syndrome	cleft palate	No
8	20 5/7	neg	R	—	—	Compomelic dysplasia	characteristic skeletal malformations	Yes
9	21 5/7	neg	R	—	—	trisomy 13	DORV, microphthalmia	Yes
10	19 2/7	neg	R	—	—	del 4q dupl 7q (unbalanced)	Tetralogy of Fallot	Yes
11	22 3/7	neg	R	—	—	trisomy 18	DORV, VSD, strawberry skull, large kidney, crossed fingers, rocker-bottom feet, enlarged CM, polyhydramnios, umbilical cord cyst	Yes
12	21 5/7	neg	R	—	—	retrognathia, VACTERL association	hemivertebrae, small stomach, hydronephrosis	No
13	27	neg	R	—	—	Pierre Robin syndrome	cleft palate, ear tag	No
14	28	neg	R	—	—	Crê-du-chat syndrome	DORV, VSD, MA, rocker-bottom foot	Yes
15	29	neg	R	—	—	Stickler syndrome	cleft palate	Yes
16	28 3/7	neg	R	—	M	Acrofacial dysostosis	IUGR, cleft palate, VSD, ventricular disproportion (L > R), small stomach, hydronephrosis, club foot, clinodactyly	No
17	19 5/7	3.7*	—	B	—	Thanatophoric dysplasia type 1	characteristic skeletal malformations without cloverleaf skull	Yes
18	20 6/7	5.5*	—	B	—	Thanatophoric dysplasia type 1	characteristic skeletal malformations without cloverleaf skull	Yes
19	21 2/7	6.3*	—	B	—	Thanatophoric dysplasia type 2	characteristic skeletal malformations with cloverleaf skull	Yes
20	32 1/7	7.4*	—	B	—	Apert syndrome	syndactyly of both hands	Yes
21	24 6/7	4.0*	—	B	—	Golfin syndrome	unilateral cleft lip and palate	Yes
22	28 6/7	2.4	—	—	—	Normal, severe dysmaturity	femur and humerus < P3	No
23	25 5/7	neg	—	—	M	microcephaly	lissencephaly, CCA, colpocephaly, cerebellar hypoplasia, CDH	No
24	21 4/7	neg	—	—	—	trisomy 13	microphthalmia, cerebellar and corpus callosum hypoplasia	Yes

Retrognathia was suspected in cases 1 to 15, in case 16, both retrognathia and a forehead anomaly were suspected and in cases 17 to 24 a forehead anomaly was suspected.

GA, gestational age in weeks. ^a, classification of PF line: 0, PF line passes parallel through the lower part of the frontal bone; neg, PF line passes the frontal bone anteriorly, when the PF line passes the frontal bone posteriorly the F distance was noted in mm.

*Enlarged F distance. ^b Confirmed after birth: R, retrognathia; B, frontal bossing; M, microcephaly; —, retrognathia or forehead anomalies absent after birth. CDH, congenital diaphragmatic hernia; AVSD, atrioventricular septum defect; LVOTO, left ventricular outflow tract obstruction; VSD, ventricular septum defect; DORV, double outlet right ventricle; CM, cisterna magna; MA, mitral atresia; IUGR, intra uterine growth retardation; CCA, corpus callosum agenesis.

Retrognathia

In retrognathia the FP line is negative, indicating that the FP line is rotated counter clockwise (when the fetus is looking to the left) by the repositioning of the mandible (Figure 2(ar)). The FP line was normal in three cases without retrognathia but with a subjective suspicion for this condition prenatally. Paladini *et al.* showed in a prospective study that when an objective measurement (jaw index) was used both sensitivity and specificity for the detection of micrognathia increased compared with subjective evaluation.⁷

Frontal bossing

When the FP line is positive before 27 weeks or the *F* distance is larger than 4 mm after 27 weeks, the frontal bone is bossing as shown by our five cases. We chose 4 mm as the upper limit of normal because the largest *F* distance in our normal population was 3.6 mm. The optimal cut-off point would need to be determined in a larger prospective study. Prognathia of the mandible might also cause an enlarged *F* distance (clockwise rotation of the FP line). We assume that this is a rather theoretical option. The combination of bossing forehead and retrognathia, may give the impression of a normal FP line; however, the combination of these anomalies is extremely rare and likely to be noticed.

Sloping forehead

In the two cases with confirmed microcephaly the FP line was negative. A fetus at 21 weeks with trisomy 13 and a head circumference at the 5th percentile also had a negative FP line (Figure 2(as)). It is tempting to assume that this fetus would have developed microcephaly. However, it may be plausible to state that the negative FP line indicated a sloping forehead meaning a disproportional growth of the skull compared with the face. Therefore, a negative FP line may indicate a sloping forehead as an early symptom of microcephaly. A sloping forehead is frequently seen in microcephaly and has been proposed as a valuable tool to recognise microcephaly; however, appropriate standardisation of this feature is still lacking.^{3,4,8,9}

Sonographers should be aware that a negative FP line may indicate a sloping forehead, retrognathia or even both. Additional investigations like neurosonography and measurements like head circumference, frontal lobe length, the MNM-angle or biometry of the mandible will be helpful to identify the underlying pathology.^{7,10–14,18} However, we believe that the FP line can be

valuable to assist the sonographer in differentiating between a normal or abnormal profile and even has the potential to identify a sloping forehead as a marker for microcephaly at an earlier stage than biometry.^{9,15,16} The FP line does not identify nose or maxilla anomalies.

Only second and third trimester fetuses from Caucasian parents were included; therefore, the results cannot be extrapolated to non-Caucasian fetuses or to the first trimester. We expect an increase in false positive cases when the line is applied in two-dimensional profiles with some deviation from the exact midsagittal plane because of the retrognathic appearance of the mandible in these cases. Caution should be used in applying the proposed FP line to profiles acquired by two-dimensional ultrasound.¹⁷

The FP line was tested retrospectively in fetuses where an anomaly was already suspected. Hence, larger studies are needed to test sensitivity and specificity of the FP line prospectively. To prevent false positives caution should be used in interpreting an abnormal FP line in the absence of other anomalies in low risk fetuses. Referral to a Fetal Medicine Unit with broad extensive experience is indicated in these cases.

In conclusion, we have shown that the FP line passes through the lower part of the forehead in almost all fetuses before 27 weeks. After 27 weeks the forehead develops a more curved appearance in about 25% of the fetuses. The FP line might be a useful tool to detect second trimester profile anomalies such as sloping foreheads, retrognathia and frontal bossing with the possibility of quantifying the latter. A negative FP line or enlarged *F* distance is suggestive of an abnormal profile and prompts further investigation to clarify the exact nature of this finding. However, findings must be interpreted carefully because larger prospective studies are needed to assess the exact sensitivity and specificity.

WHAT'S ALREADY KNOWN ABOUT THIS TOPIC?

- Fetal profile anomalies are associated with a wide range of genetic conditions and syndromes.

WHAT DOES THIS STUDY ADD?

- It is likely that the Fetal Profile line may improve the prenatal detection of retrognathia, sloping foreheads and frontal bossing.
- The Fetal Profile line is the first objective tool for assessing sloping foreheads and quantifying bossing foreheads.

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